

## REMARKS

At the outset, Applicants wish to thank the Examiner for taking time from her busy schedule to hold a telephonic interview with Applicants' undersigned representative on August 10, 2004.

### I) Claim Objections

The Examiner has objected to the claims on several grounds. Applicants have amended the claims<sup>1</sup> to address each of these objections and respectfully request the objections be withdrawn.

- A) The Examiner objected to the term “a LINEAGE marker” in claims 1, 23, and 32. The phrase has been deleted from each of the claims.<sup>2</sup>
- B) The Examiner objected to claims 7, 24, and 33 as being improper dependent claims. Claims 7, 24, and 33 have been cancelled.
- C) Claim 23 is objected to for use of the incorrect amendment format. Claim 23 is amended in the present amendment, using the proper format: “currently amended.”
- D) The Examiner has requested that the term “stem” be inserted after “tumor” in claim 32. This phrase has been deleted from the claim with newly added language using the phrase “tumor stem” as requested.
- E) The Examiner has objected to the use of the term “lectin” in claim 34. Applicants have deleted this term from claim 34.<sup>3</sup>
- F) Claims 187 and 198 are objected to as being duplicates of claims 6 and 194. Applicants have cancelled claims 187 and 198.

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<sup>1</sup> Applicants do not necessarily agree that the claims need to be amended, but do so to further the prosecution of the present application and reserve the right to pursue claims having the original language (or similar language) in the future.

<sup>2</sup> Applicant note a factual inaccuracy in the Examiner's objection. Contrary to the Examiner's assertion, some sarcomas are of epithelial origin, and thus are within the claim scope of the presently amended claims. See e.g., Leyvraz S, Costa J: Histological diagnosis and grading of soft-tissue sarcomas. *Semin Surg Oncol* 4:3–6, 1988.

<sup>3</sup> Applicants note that the claims of the present invention, while not reciting “lectin,” still encompass the use of lectins in the claimed methods.

- G) Claim 200 is objected to for lacking a space in the phrase “claim 1.” Applicants have added a space.

## II) The Claims are Definite

The Examiner has rejected the claims as allegedly being indefinite. Applicants have amended the claims to address these rejections.<sup>4</sup>

A) The Examiner has rejected the use of the term 75% free because of alleged confusion as to how this term pertains to individual cells. Applicants respectfully disagree. However, the claims have been amended to specify “populations” of cells that contain the recited percentages or amounts of solid tumor stem cells.

B) The Examiner has rejected claim 1 for allegedly lacking antecedent basis for the phrase “said isolated solid tumor stem cell” and for allegedly being indefinite for using the phrase “that fail the requirements of . . . .” Applicants have amended claim 1 to remove the rejected language.

C) The Examiner has rejected claim 32 for use of the phrase “solid tumor stem cell positive marker CD44” and has requested deletion of the phrase “solid tumor stem cell positive marker” to obviate the rejection. Applicants have deleted the phrase as suggested by the Examiner.

In view of the above, Applicants request that the 35 U.S.C. § 112, second paragraph, rejections be withdrawn. Applicants note that, upon withdrawal of these rejections, claims 32-35, 38, 40, 188, 204, and 205 are allowable as they are not rejected on any other grounds.

## III) The Claimed Subject Matter is Novel and Non-obvious

The Examiner has rejected the claims (other than claims 32-35, 38, 40, 188, 204, and 205) as allegedly being anticipated and/or obvious in view of Salmon et al. (“Salmon”), Hartman et al. (“Hartman”), Martin et al. (“Martin”), Schlom et al. (“Schlom”), Nierodzik et al. (“Nierodzik”), Jeffries et al. (“Jeffries”), and Bromberg et al. (“Bromberg”), either alone, or in various combinations. Applicants respectfully disagree.

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<sup>4</sup> Applicants do not agree that the claims need to be amended, but do so to further the prosecution of the present application and reserve the right to pursue claims having the original language (or similar language) in the future.

**A) The Examiner's rejections did not consider the "isolated"/"enriched" element**

Because the Examiner asserted that the isolation element was indefinite, the Examiner did not consider this element in assessing the cited documents ("the '75%' limitation in claim 1 has not been considered for reasons discussed under 35 U.S.C. 112, 2<sup>nd</sup> paragraph", Office Action, page 8). As discussed above, Applicants have amended claim 1 to clarify that the claim is directed to a population of cells that contain less than 25% non-tumorigenic solid tumor cells and that the tumorigenic solid tumor stem cells in the population have the specific recited properties. Applicants have also amended claim 23 to recite that the claimed population of cells be enriched at least 2-fold in cells having the recited properties.

When the isolation/enrichment element is considered, the rejections must be withdrawn, as the cited documents do not teach or suggest isolated or enriched populations of cells having the recited properties (e.g., populations of tumorigenic stem cells that are isolated/enriched relative to non-tumorigenic tumor cells).

Martin used a technique to enrich for tumor cells relative to non-tumor cells, but does not enrich for tumorigenic stem cells from other solid tumor cells as recited in the claims. Nothing in the methods of Martin suggest any ability to isolate or enrich for tumorigenic stem cells relative to other tumor cells. Thus, the "enriched" cells of Martin appear to not be isolated or enriched at all from other solid tumor cells, but instead constitute a mixture of tumorigenic and non-tumorigenic cells, apparently in the same ratio as found in the original solid tumor. Thus, Martin, alone or in combination with the other cited documents, does not anticipate or render obvious the presently claimed invention.

Salmon does not teach or suggest isolated populations having less than 25% non-tumorigenic solid tumor cells or populations enriched at least 2-fold in tumorigenic solid tumor stem cells having the recited properties. Nothing in Salmon or the other cited documents teaches or suggests a combination of markers that would permit one to achieve such isolated/enriched within a population of cells. Thus, this document, alone

or in combination with the other cited documents does not anticipate or render obvious the presently claimed invention.

Nierodzik does not teach or suggest isolated populations, isolated from a solid tumor, having less than 25% non-tumorigenic solid tumor cells or populations enriched at least 2-fold in tumorigenic solid tumor stem cells having the recited properties. Thus, Nierodzik, alone or in combination with the other cited documents does not anticipate or render obvious the presently claimed invention.

Because the primary documents, Salmon, Martin, and Nierodzik, fail to teach each of the elements of the present invention, and because the secondary documents cited in the obviousness rejections do not remedy the deficiencies, the claims must be passed to allowance.

**B) The Product-by-Process Claims Specify A Novel Composition**

The method claims of the present invention are novel and non-obvious. This point is not in dispute. Thus, the cited documents do not teach or suggest contacting tumor cells with the recited reagents to identify and/or isolate cells expressing particular combinations of markers. A product-by-process composition claim is patentable when the resulting composition derived from the method is not found in the cited documents (e.g., obtained by other methods). This is unquestionably the case for the present claims.

To clarify this point, claim 199 has been amended to recite that the enriched population of solid tumor stem cells is isolated by the method of claim 40. The identity of cells in a population enriched by the recited method will be specific for the particular reagents used. Thus, the population is itself necessarily novel and nonobvious due to the specific population of cells selected for by the recited method. None of the documents cited by the Examiner teach or suggest the claimed enriched population of cells isolated by the recited method. Thus, the product-by-process composition claims of the present invention are novel and non-obvious and the rejection of claim 199 must be withdrawn.

For the reasons discussed above, Applicants respectfully request that the anticipation/obviousness rejections be withdrawn.

For thoroughness, Applicants bring to the Examiner's attention U.S. Pat. Publ. No. 2003/0119080A1, entitled "Strategies for the Identification and Isolation of Cancer

Stem Cells and Non-Cancerous Stem Cells,” which is not prior art against the present application.

### CONCLUSION

All grounds of rejections and objections have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that the claims as amended should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of the captioned application, Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

Dated: \_\_\_\_\_

8/24/04



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